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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,913	11/18/2005	Larry Hench	YOUZ 2 00108	5223
27885	7590	10/16/2006	EXAMINER	
FAY, SHARPE, FAGAN, MINNICH & MCKEE, LLP 1100 SUPERIOR AVENUE, SEVENTH FLOOR CLEVELAND, OH 44114			SHEN, BIN	
			ART UNIT	PAPER NUMBER
			1657	

DATE MAILED: 10/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/520,913

Applicant(s)

HENCH ET AL.

Examiner

Bin Shen

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1655

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-19, 24 and 26 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-19, 24 and 26 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: ____.

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DETAILED ACTION

The IDS received 11/18/2005, the preliminary amendment received 11/18/2005 have been entered.

Claims 1-19, 24 and 26 are presented for examination on the merits.

Specification

1. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

2. The uses of the trademark "Bioglass" on pages 8, 11, 12, 15, 19, 20, have been noted in this application. They should be capitalized wherever they appear and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps,

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such omission amounting to a gap between the steps. See MPEP § 2172.01. Claim 1 is incomplete because it lacks a correlating step to accomplish the preamble of the claim. The claims drawn to a method of eliciting a Raman signal with a single step of irradiating the cell with a laser, however this one step does not complete the method. The omitted steps are: collecting and analyzing spectra emitted from the laser irradiated cell.

4. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 18 is rendered vague and indefinite by the phrase "induced by ... a cytotoxic agent, protein levels ... cell cycle" because the claim do not distinguish between two different categories- i.e. agents and their effects (changes in protein levels, DNA ...), it is suggested that claim 18 be amended to recite -induced by a pharmaceutical agent or a cytotoxic agent, wherein the cell phenotype include protein levels, DNA or RNA levels, the extracellular matrix, the cell cycle--.

All other claims depend directly or indirectly from rejected claims are, therefore, also rejected under USC 112, second paragraph for the reasons set forth above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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5. Claims 1-2, 7-8, 17-19 rejected under 35 U.S.C. 102(b) as being anticipated by Chaiken et al. (USPN6352502).

Chaiken et al. teach a method of eliciting a Raman signal (including many parameters related with living cell such as information on nucleic acid, protein, lipid-see col. 14, lines 20-23) using Raman spectroscopy from a living cell/tissue by irradiating a cell/tissue with a laser having a wavelength of 785 nm (see claim 1, and also col. 1 lines 16-19, Fig.1 and col. 8, lines 46, claims 6-7) at an intensity of 50-300 mW (col. 8, line 66-col. 9. line 11), detecting abnormalities (read as changes) in living cell (col. 14, line 43-60) over a period of time, where the abnormalities/changes include cancers (read as cell growth) by detecting increase in phosphorous-containing bonds (as are abundant in nucleic acid such as DNA and RNA), and the method can be used to detect substance/chemicals that brought into contact with the living cell (col. 14, line 61-col. 15, line 11).

Therefore, the cited reference is deemed to anticipate the instant claims above.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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6. Claims 1-14, 17-19, 24, 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chaiken et al., in view of WO0151094A1, and further in view of Puppels et al. (Biophysical Journal 1991;60:1046-1056.

Chaiken et al. teach what is above.

Chaiken et al. do not teach the total energy and time of irradiating the cell with laser, the focusing of cytoplasm, nucleus and extracellular matrix of the cell, and the detection of cell cycle and cell death.

WO teaches a method of performing Raman spectroscopy of a living cell, or a plurality of living cell (read as tissue) after infrared laser beam (can be at 785 nm, see page 21, line 1) irradiating (page 2, lines 24-29) at maximum total power of 300-700 mW (page 21, line 4) for a period of up to 40 minutes (page 25, line 15). According to calculation (see attached Joule definition and conversions where 1 watt-hour=3600 Joules), 4 successive 400 seconds (read on as "up to 40 minutes" see page 25, line 15) measurements at a power of between 300 to 700 mW yield a total energy of between 480 to 1120 Joules.

Puppels et al. teach the use of Raman microspectroscopic approach (see abstract) to record spectra of nuclei and cytoplasmic regions of living human cells (granulocytes) attached to a poly-L-lysine coated substrates (page 1049, 1st paragraph, line 15), DNA-protein ratio are determined by the nucleus spectrum which reflect the state of the chromatin structure (page 1048, paragraph under "Determination of DNA-protein ratio" and also page 1049, lines 24-30), DNA structure are also examined (see page 1050, 1st full paragraph).

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It would have been obvious to one of ordinary skill in the art at the time the invention was made to choose the appropriate laser light intensity, the laser wavelength, and the measurement times to eliciting a Raman signal from a living cell as taught by Chaiken et al. because Puppels teach that cell viability is a matter of concern which poses limitations on the laser light intensity, wavelength, and the measurement times that can be employed (page 1046, 2nd paragraph, lines 4-7). One would have been motivated to choose the appropriate irradiation conditions to study the different cell organelles including cytoplasm, nucleus and extracellular matrix because Cheiken et al. teach the importance for qualitative/quantitative noninvasive assessment of the metabolic and structural components of living cell and its surrounding cells using Raman spectroscopy (col. 1 lines 16-19), and that information from cytoplasm, nucleus, and extracellular matrix constitute important parts of cell metabolic state, and would reasonably have expected success because Puppels et al. teach the use of Raman spectroscopy as a powerful method to investigate nuclei and cytoplasmic regions of single living cells. It would have been obvious to one of ordinary skill in the art at the time the invention was made to detect cell cycle and cell death (similar to cell growth as discussed above) by Raman spectroscopy characterization of biological molecules such as DNA, RNA, proteins because cell cycle is characterize by the chromatin structure changes during mitosis and cell death is characterize by fragmentation of DNA (see page 17 of the specification), and both DNA structure changes can be detected by Raman spectroscopy as taught by Puppels.

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7. Claims 1, 2, 7, 8, 13-16, 17-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chaiken et al., in view of Puppels et al., and further in view of Sepulveda et al. (J Biomed Mater Res 2002;61:301-311).

Chaiken et al. teach what is above.

Puppels et al. teach what is above.

Chaiken and Puppels et al. do not teach the use of a bioactive glass or a sol-gel derived gel glass.

Sepulveda et al. teaches the use of bioactive glass 45S5 (same material used in the examples of the specification) in vitro and that sol-gel derived silica-containing bioactive glasses are more bioactive (see page 301, middle of the 1st full paragraph), and provide scaffolds for tissue engineering (see page 302, left column, lines 2-7; also see page 15, lines 1-4 of the specification for the use of bioactive glasses for tissue engineering purpose).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use sol-gel derived bioactive glass to culture cell in the method of Chaiken et al. because Puppels teach the importance of cell viability during Raman spectroscopy and Sepulveda teach that bioactive glass promote cell proliferation/growth (page 310, end of 1st paragraph). One would have been motivated to use bioactive glasses to culture cell in the method of Chaiken et al, because Puppels et al. also teach the use of the poly-L-lysine coated substrates in cell culture to insure the reproducibility of the Raman spectra, and would reasonably have expected success because Sepulveda et al. teach the use of bioactive glasses for producing scaffolds for tissue engineering which will improve

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cell viability and contribute to higher reproducibility of the Raman spectra (as taught by Puppels).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

8. No claim is allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily

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Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Bin Shen, Ph.D., whose telephone number is (571) 272-9040. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to her office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Terry McKelvey can be reached at (571) 272-0775.



MICHAEL MELLER
PRIMARY EXAMINER

B Shen

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